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ATTORNEY DOCKET No.: 2003946-0148 (PITA/US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Agoulnik *et al.* Examiner: NYA.  
Serial No: 10/501,120 Group Art Unit: NYA  
Filing Date: July 8, 2004  
Corresp. to: PCT/US03/00390  
Int. Filing Date: January 8, 2003  
Earliest Priority: January 8, 2002  
Title: EPONEMYCIN AND EPOXOMICIN ANALOGS AND USES THEREOF


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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

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October 25, 2004  
Date

  
Signature  
Kathy Hart Gagnon

Typed or Printed Name of person signing certificate

Sir:

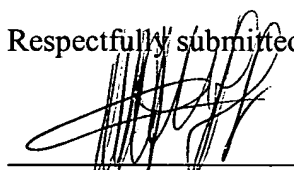
## TRANSMITTAL

In regard to the above-referenced patent application, enclosed please find the following:

1. Statement Filed Pursuant To The Duty Of Disclosure Under 37 CFR §§ 1.56, 1.97 and 1.98 (6 pp.);
2. Supplemental Form PTO-1449 (1 pg.);
3. Cited Art (7 references); and
4. Return-Receipt Postcard.

If any additional fees are required to be paid or if any overpayment has been made, please charge same to Deposit Account No. 03-1721.

Respectfully submitted,



Dated: October 25, 2004

Nadège M. Lagneau, Ph.D.  
Agent for Applicant  
Reg. No. 51,908

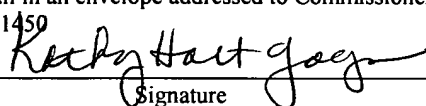
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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**STATEMENT FILED PURSUANT TO THE  
DUTY OF DISCLOSURE UNDER 37 CFR §§ 1.56, 1.97 AND 1.98**

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, Applicant requests consideration of this Information Disclosure Statement.

Type of Statement

The present Information Disclosure Statement is:

- ☐ An *original* Information Disclosure Statement; or  
☒ A *supplemental* Information Disclosure Statement.

The present Information Disclosure Statement is being filed:

- ☒ Pursuant to 37 CFR § 1.97(b); no fee or certification is required:
  - ☐ Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
  - ☐ Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
  - ☒ Before the mailing of a first Office action on the merits; or
  - ☐ Before the mailing of a first Office action after the filing of a request for continued examination under § 1.114.
- ☐ Pursuant to 37 CFR § 1.97(c) after the dates listed above but before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *either*:
  - ☐ Certifies that *either*:
    - ☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
    - ☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making

reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; or

☐ Includes herewith the fee set forth in § 1.17(p).

☐ Pursuant to 37 CFR § 1.97(d), after the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *both*:

☐ Certifies that *either*:

☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; and

Content of the Information Disclosure Statement

Applicant hereby makes of record in the above-identified application the reference(s) listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

Applicant includes copies of references as indicated below:

- ☒ A copy of each cited reference not indicated with a † is included;
- ☐ Copies of references indicated with an asterisk on the attached form PTO-1449 are not included pursuant to 37 CFR § 1.98(d) because they were previously provided to the United States Patent Office in an Information Disclosure Statement that complies with 37 CFR § 1.98(a)-(c) and was submitted in the following patent application that is relied upon in the present case for an earlier effective filing date under 35 USC § 120:

Serial Number	Filing Date	Status

- ☐ Copies of English translations of one or more non-English references are included.

Applicant hereby makes the following additional information of record in the above-identified application:

Applicant certifies that the Information Disclosure Statement *either*:

- ☒ Does not contain non-English language citations;
- ☐ Does contain non-English language citations, of which an English language translation of the Abstract for each is provided herein:

[ ] Includes one or more translations of a non-English citation.

Remarks

The submission of this Information Disclosure Statement should not be construed as a representation that a search has been made.

The submission of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in § 1.56(b) .

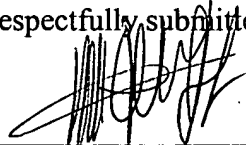
The submission of this Information Disclosure Statement shall not be construed as a representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited patent(s) and publication(s) has (have) been fully considered by the Patent and Trademark Office during the examination of this application; and
3. The citations for the patent(s) and publication(s) be printed on any patent which issues from this application.

Notwithstanding any statements by Applicants, the Examiner is urged to form his or her own conclusions regarding the relevance of the cited reference(s).

Respectfully submitted,



---

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Reg. No. 51,908

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Boston, Massachusetts 02109  
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Fax: (617) 248-4000

Dated: October 25, 2004

<b>Form PTO-1449</b> <b>(REV. 8-03)</b>		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket 2003946-0148 (PITA/US)		In re Application No. 10/501,120	
<b>SUPPLEMENTAL INFORMATION</b> <b>DISCLOSURE STATEMENT</b> <i>(Use several sheets if necessary)</i>				Applicant: AgoulNIK <i>et al</i>			
				Filing Date: July 8, 2004		Group: NYA	
<b>U.S. PATENT DOCUMENTS</b>							
Examiner's Initials	U.S. Patent No.	Applicant	Issue Date	Class	Subclass		
<b>U.S. PATENT APPLICATIONS</b>							
Examiner's Initials:	Serial Number:	Applicant:	Filing Date:	Group:	Art Unit:		
<b>FOREIGN PATENT DOCUMENTS</b>							
Examiner's Initials	Document No.	Country	International Publication Date	Translation			
				Yes	No		
<b>OTHER DOCUMENTS</b>							
Examiner's Initials	Citation (Including Author, Title, Date, Pertinent Pages, Etc.)						
✓	Hanada, et al., "Epoxomicin. A New Antitumor Agent Of Microbial Origin", <i>Journal of Antibiotics</i> , <b>45</b> (11): 1746-1752, 1992.						
✓	Koguchi, et al., "TMC-86A, B and TMC-96, New Proteasome Inhibitors from <i>Streptomyces</i> sp. TC 1084 and <i>Saccharothrix</i> sp. TC 1094 II. Physico-chemical Properties and Structure Determination", <i>Journal of Antibiotics</i> , <b>53</b> (1): 63-65, 2000.						
✓	Koguchi, et al., "TMC-89A and B, New Proteasome Inhibitors from <i>Streptomyces</i> sp. TC 1087", <i>Journal of Antibiotics</i> , <b>53</b> (9): 967-972, 2000.						
✓	Meng, et al., "Eponemycin Exerts Its Antitumor Effect through the Inhibition of Proteasome Function <sup>1</sup> ", <i>Cancer Research</i> , <b>59</b> : 2798-2801, 1999.						
✓	Meng, et al., "Epoxomicin, a potent and selective proteasome inhibitor, exhibits <i>in vivo</i> antiinflammatory activity", <i>Proc. Natl. Acad. Sci. USA</i> , <b>96</b> : 10403-10408, 1999.						
✓	Myung, et al., "The Ubiquitin-Proteasome Pathway and Proteasome Inhibitors", <i>Medicinal Research Reviews</i> , <b>21</b> (4): 245-273, 2001.						
	Sugawara, et al., "Eponemycin <sup>†</sup> A New Antibiotic Active Against B16 Melanoma I. Production, Isolation, Structure And Biological Activity", <i>Journal of Antibiotics</i> , <b>XLIII</b> (1): 8-18, 1990.						
<b>EXAMINER</b>			<b>DATE CONSIDERED</b>				
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							